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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/092,367 | 03/07/2002 | Baldomero M. Olivera | 2314-224-II | 7797 |
| 6449 | 7590 | 06/22/2004 | EXAMINER | |
| ROTHWELL, FIGG, ERNST & MANBECK, P.C. 1425 K STREET, N.W. SUITE 800 WASHINGTON, DC 20005 | | | KAM, CHIH MIN | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1653 | |

DATE MAILED: 06/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|--------------------------------------|---------------------------------------|--|
| Office Action Summary | Application No. 10/092,367 | Applicant(s) OLIVERA ET AL. | |
| | Examiner Chih-Min Kam | Art Unit 1653 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 April 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,5 and 25-29 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2 and 25-28 is/are rejected.
- 7) ☒ Claim(s) 5 and 29 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>12/11/02</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Election/Restrictions

1. In the amendment and response to restriction filed April 7, 2004, Applicant has elected Group I, claims 1, 2, 5 for examination. Applicants also provisionally elect the peptide Bt5 having an amino acid sequence set forth in SEQ ID NO:6 (genus) and SEQ ID NO:138 (species), and the corresponding propeptide of SEQ ID NO:73 with traverse. In the amendment, claims 1 and 5 have been amended, claims 3, 4, and 6-24 have been cancelled, and new claims 25-29 have been added, therefore claims 1, 2, 5 and 25-29 are pending. The traversal is on the ground(s) that the search and examination of all the peptides (65 sequences) can be made without serious burden. Applicants indicate the instant application relates to linear γ -carboxyglutamate rich conotoxins, which each has at least three γ -carboxyglutamate residues, thus each sequence given in the claims represents a species of the γ -carboxyglutamate rich conotoxin genus, and since all the species share a common structural motif, applicants believe the restriction between various species of this genus is unwarranted. Applicants also indicates the criteria for restriction practice relating to Markush-type claims are set forth in MPEP 803.02. If the members of the Markush group are sufficiently few in numbers or so closely related that a search and examination of the entire claims can be made without serious burden, the Examiner must examine all claims on the merits, even though they are directed to independent and distinct inventions. Applicants further assert that various conopeptides may be distinct from each other, however, distinctness alone is not enough to require a restriction, there must be a serious burden on the examiner, and it is urged that the burden of examining all the peptide claims of the present application is not serious burden in

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various aspects regarding utility under 35 U. S. C. §101, 35 U. S. C. §112, first and second paragraphs, review of prior art to determine whether the claims are anticipated or obvious because all peptides are all related in their structure and biological activity, the wording of the claims in each group of claims is identical except for the specified peptide, the search for the scientific literature or the patent and the review of the prior art literature and patents will be identical for all the peptides, and the computer search based on the peptide sequence in the sequence listing would identify prior art directed to the claimed peptides or peptides having the specified substituents. Consequently, no additional search is required to examine all the peptides or related propeptides, thus no undue burden exists in this instance (pages 7-12 of the response). The response has been considered, however, the argument is not found persuasive because the traversal is not on the grounds that the inventions are not independent and distinct, rather, the traversal is on the grounds that there is no burden of search to include all the sequences. As such restriction is proper if two or more claimed inventions are either independent or distinct. See MPEP 803. As indicated in the restriction requirement, each conotoxin peptide, which contains different amino acid sequence, exhibits different physical and chemical properties, and has different effect, is patentably distinct. This distinctness of each conotoxin peptide is evident in the analogs of conantokin-G (Zhou *et al.*, J. Neurochemistry 66, 620-628 (1996)). Zhou *et al.* disclose various analogs of conantokin-G (Gly-Glu-Gla-Gla-Leu-Gln-Gla-Asn-Gln-Gla-Leu-Ile-Arg-Gla-Lys-Ser-Asn-NH₂), which have γ -carboxyglutamate (Gla) substituted with Ala, Ser or phosphoserine at various positions, show different N-methyl-D-aspartate (NMDA) antagonist activities. Since each conotoxin peptide is patentably distinct from each other, the restriction

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between different conotoxins is proper, thus the election of a specific conotoxin peptide is not a species election. In addition to the text search in patents or literature regarding conotoxins, each claimed peptide has to be searched independently due to its distinctness, thus coexamination of total 65 sequences (32 sequences in claim 1, 32 sequences in claim 5, and 1 sequence in claim 27) would require additional sequence search other than the search on the elected sequence. In the sequence search, each sequence is searched against 6 data files, thus, total 390 (65 x 6) data files need to be searched and reviewed. In view of numerous data resulted from sequence search, coexamination of all peptide sequences would require a serious burden of search and examination on the examiner. Therefore, claims 1, 2, 5 and 25-29, and the elected conotoxin Bt5 of SEQ ID NO: 6 and 138, and propeptide SEQ ID NO:73 are examined, all other conotoxins are non-elected sequences and withdrawn from consideration.

The requirement is still deemed proper and is therefore made FINAL.

Oath/Declaration

2. The oath or declaration filed June 4, 2002 is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. The oath or declaration is defective because non-dated alteration has been made to the citizenship of inventor Baldomero M. Olivera. See 37 CFR 1.52(c).

Informalities

The disclosure is objected to because of the following informalities:

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3. The specification (e.g., at page 1, line 30; page 9, line 29) cites embedded hyperlinks and/or other forms of browser-executable code, which are impermissible and require deletion. Appropriate correction is required.

Claim Objections

4. Claims 1, 2 and 5 are objected to because the claim contains recitation of non-elected sequences and amino acid variables in the non-elected sequences. Claim 1 is also objected to because a symbol “^” is indicated after the sequence.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1, 2 and 25-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
6. Claims 2, 26 and 28 are indefinite because claims 2, 26 and 28 do not further limit the scope of the claim they are dependent from, e.g., claim 1 is directed to the amino acid sequence of Conotoxin-Bt (SEQ ID NO:6), however, claim 2 is directed to a derivative of the claimed sequence, which has a broader scope than claim 1.
7. Claims 1, 2, and 25-28 are indefinite because of the use of the term “nor-Lys”, “nor-Tyr”, “neo-Trp”, “Hyp”, “may be substituted”, “may be glycosylated”, “any synthetic hydroxy containing amino acid”, “O-sulpho- and O-phospho-derivatives”, or “synthetic derivatives bearing non-natural aliphatic branched or linear side chains C_nH_{2n+2} up to and including $n=8$ ”,. The term “nor-Lys”, “nor-Tyr” or “neo-Trp” renders

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the claim indefinite, it is unclear what structure the "nor-Lys", "nor-Tyr" or "neo-Trp" has, since a search of these terms in STN registry file does not have any hit. As to the term "may be substituted", it is unclear, for example, whether Arg is substituted by Lys, ornithine, homoarginine, nor-Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any synthetic basic amino acid, or, it is not substituted, or, it is substituted by anything else as to "the Arg residues may be substituted by Lys,or any synthetic basic amino acid". As to the term "may be glycosylated" or "Hyp", it is unclear whether Asn, Ser, Thr or Hyp is glycosylated or not, and what the term "Hyp" means. A fully spelled word for "Hyp" should be indicated. As to "any synthetic hydroxy containing amino acid", it is unclear how a hydroxy group would contain amino acid, use of the term "any synthetic hydroxy-containing amino acid" is suggested. As to the term "O-sulpho- and O-phospho-derivatives" or "synthetic derivatives bearing non-natural aliphatic branched or linear side chains C_nH_{2n+2} up to and including $n=8$ ", it is not clear what structure the O-sulpho-derivative, O-phospho-derivative or the synthetic derivative has, and how different the derivative is from the parent compound since neither the specification nor the claim defines the term. Claims 25 and 27 are included in the rejection because they are dependent on a rejected claim and do not correct the deficiency of the claim from which they depend.

8. Claim 29 is objected to as being dependent upon an objected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

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Conclusion

9. Claims 1, 2 and 25-28 are rejected, and claims 5 and 29 are objected to.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D.
Patent Examiner



June 21, 2004